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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/695,846	10/29/2003	Sean Philpott	454311-2220.2	7869
20999	7590	10/17/2006	EXAMINER	
FROMMER LAWRENCE & HAUG 745 FIFTH AVENUE- 10TH FL. NEW YORK, NY 10151			HUMPHREY, LOUISE WANG ZHIYING	
			ART UNIT	PAPER NUMBER
			1648	
DATE MAILED: 10/17/2006				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/695,846

Applicant(s)

PHILPOTT ET AL.

Examiner

Louise Humphrey, Ph.D.

Art Unit

1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 September 2006.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 20-116 is/are pending in the application.
- 4a) Of the above claim(s) See Continuation Sheet is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) See Continuation Sheet is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 29 October 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>10/29/03</u> . | 6) <input type="checkbox"/> Other: _____ |

Continuation of Disposition of Claims: Claims withdrawn from consideration are 20-29,33-53,58,59,64,65,70,71,74,75,78,79,82,83,87,88,90-92,96,97,99-101,105,106,108-110,115 and 116.

Continuation of Disposition of Claims: Claims rejected are 30-32,54-57,60-63,66-69,72,73,76,77,80,81,84-86,89,93-95,98,102-104,107 and 111-114.

DETAILED ACTION

The Office acknowledges the receipt of Applicant's election and Amendment, filed on 18 September 2006.

Election/Restriction

Applicant elects Group II, claims 30-32 and 54-110, with traverse. The traversal is on the grounds that there is no serious search burden in examining the different Groups together and that the species are the members of a Markush group. Applicant's traversal is unpersuasive for the following reasons:

Applicant's traversal with regards to search burden is based upon the classification number assigned to each Group. The PTO classification is merely an administrative convenience and is not dispositive of the relatedness of applications. There are different limitations in each Group that require a separate search. Even if the Groups were placed in the same class and subclass, the searches are not co-extensive and thus would be an undue burden on Office resources.

Applicants' citation of MPEP §803 in addressing the species election is improper because each antiretroviral therapy is not considered to be a proper member of a Markush group. See M.P.E.P. § 803.02. *In re Harnish*, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and *Ex parte Hozumi*, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Broadly, unity of invention exists where compounds included within a Markush group (1) share a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility. The instant claims are drawn to multiple antiretroviral therapies, which are considered to be unrelated, since each therapy claimed is structurally and

Art Unit: 1648

functionally independent and distinct. As such, the therapies in the instant claims are not considered to constitute a proper Markush group/genus, and are therefore subject to restriction. In view of the foregoing, one therapy is considered to be a reasonable number for examination.

Furthermore, Applicants elected the genus as exemplified by claim 89 for examination instead of the individual species respectively recited in claims 90-92. Examiner will select anyone of the species in the "the group consisting of highly active antiretroviral therapy (HAART), protease inhibitors, fusion inhibitors, integrase inhibitors, coreceptor specific agents, non-nucleoside analogue reverse transcriptase inhibitors and nucleoside analogue reverse transcriptase inhibitors" will be examined.

It is noted that Applicant is no longer entitled to the rejoinder of the process claims with the product claims in light of *In re Ochiai* and *In re Brouwer* because Applicant has elected the process claim. See M.P.E.P. §821.04.

The restriction between the claimed product and methods is maintained. The requirement is still deemed proper and is therefore made FINAL.

Claims 20-116 are pending. Claims 20-29, 33-53, 58, 59, 64, 65, 70, 71, 74, 75, 78, 79, 82, 83, 87, 88, 90-92, 96, 97, 99-101, 105, 106, 108-110, 115 and 116 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention and species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 18 September 2006. Claims 30-32, 54-57, 60-63, 66-69, 72, 73, 76, 77, 80, 81, 84-86, 89,

Art Unit: 1648

93-95, 98, 102-104, 107, and 111-114 are examined to the extent that they read on the elected species.

Information Disclosure Statement

An initialed and dated copy of each of Applicant's IDS form 1449, filed on 29 October 2003, is attached to the instant Office action.

Specification

Applicant is required to update the status (pending, allowed, etc.) of all parent applications in the first line of the specification. The status of all citations of US filed applications in the specification should also be updated where appropriate.

Double patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Art Unit: 1648

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 30-32, 54-57, 60-63, 66-69, 72, 73, 76, 77, 80, 81, 84-86, 89, 93-95, 98, 102-104, 107, and 111-114 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-57 of U.S. Patent No. 6,727,060. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are anticipated by the patented claims. Both sets of claims are drawn to methods of essentially the same steps, which overlap in scope between the two applications.

Claim Rejections - 35 USC § 112, 2nd ¶

The following is a quotation of the second paragraph of 35 U.S.C. §112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 30-32, 54-57, 60-63, 66-69, 72, 73, 76, 77, 80, and 81 are rejected under 35 U.S.C. §112, second paragraph, as being vague and indefinite because there is no recitation of any active method step that is entailed in the claimed process. Applicants can obviate this rejection by amending the claims to include method steps such as assaying the patient-derived HIV sample; determining CXCR4 and CCR5 co-receptor use. Clarification and/or correction are required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 30-32, 54-57, 60-63, 66-69, 72, 73, 76, 77, 80, 81, 84-86, 89, 93-95, 98, 102-104, 107, and 111-114 are rejected under 35 U.S.C. §103(a) as being unpatentable over Esté *et al.* (reference no. AL on page 2 of the IDS) in view of Bazan *et al.* (1998).

The instant invention is a diagnostic method comprising determining CXCR4 coreceptor use, CCR5 coreceptor use, and a ratio of acquired immunodeficiency virus using the CXCR4 coreceptor compared to virus using the CCR5 coreceptor.

Esté *et al.* disclose that bicyclam AMD3100 is a potent inhibitor of X4 HIV strains and selects for the outgrowth of R5 virus after cultivation of mixtures of the laboratory-adapted R5 (Bal) and X4 (NL4-3) HIV strains in the presence of the compound. The addition of AMD3100 to peripheral blood mononuclear cells infected with X4 or R5X4 clinical HIV isolates displaying the syncytium-inducing phenotype resulted in a complete suppression of X4 variants and a concomitant genotypic change in the V2 and V3 loops of the envelope gp120 glycoprotein. The recovered viruses corresponded genotypically and phenotypically to R5 variants in that they could no longer use CXCR4 as coreceptor or induce syncytium formation in MT-2 cells. Furthermore, the phenotype and genotype of a cloned R5 HIV-1 virus converted to those of the R5X4 virus after prolonged culture

Art Unit: 1648

in lymphoid cells. However, these changes did not occur when the infected cells were cultured in the presence of AMD3100, despite low levels of virus replication (Abstract and page 5583). Esté *et al.* further suggest that CXCR4 antagonists could be intended as deterrents for the emergence of X4 strains, more than to decrease viral load levels, which can be effectively achieved by triple drug combinations of reverse transcriptase inhibitors and protease inhibitors. The concurrent observations that they have made with both laboratory HIV strains and clinical HIV isolates point to the potential usefulness of CXCR4 antagonists in preventing the switch from R5 to X4 that is generally considered a hallmark of the onset of AIDS and/or the progression of the disease (page 5584, left column). Esté *et al.* specifically disclose a method of determination of viral fitness in a mixed virus population isolated from peripheral blood mononuclear cells (PBMC) in the presence or absence of an antiretroviral therapeutic agent, AMD3100 (pages 5578-5579). They demonstrate that, in the presence of AMD3100, only the BaL strain was detected in the proviral DNA even at the highest NL4-3/BaL ratio in the infecting virus mixture (80% NL4-3 to 20% BaL)(Fig. 1).

Esté *et al.* does not disclose a patient-derived HIV primary isolate for the monitoring assay.

Bazan *et al.* suggest using diverse primary HIV isolates for coreceptor usage assays. Specifically, Bazan *et al.* examine molecularly cloned Env from a panel of primary HIV-1 isolates representing diverse phenotypes and genetic subtypes (clades). These isolates were collected at epicenters of the global AIDS pandemic by the World Health Organization and National Institute of Allergy and Infectious Diseases Networks

Art Unit: 1648

for HIV Isolation and Characterization, with the goal of generating a panel of naturally occurring primary strains to facilitate structure and function studies and vaccine development (page 4485, left column, 2nd ¶).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to substitute the laboratory isolates of Esté *et al.* with the patient-derived primary isolates taught by Bazan *et al.* The skilled artisan would have been motivated to do so to apply the method to natural viruses for a better assessment of the efficacy of HIV therapy in the clinical setting. There would have been a reasonable expectation of success, given the availability of a panel of primary HIV-1 isolates collected by the WHO and NIAID, as taught by Bazan *et al.* Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Remarks

No claim is allowable.

Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP §714.02 and §2163.06.

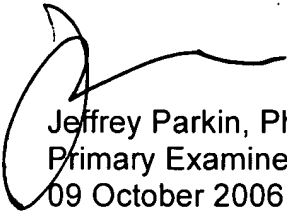
Art Unit: 1648

Contact Information


Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey, Ph.D. whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9:30 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



Jeffrey Parkin, Ph.D.
Primary Examiner
09 October 2006


10/9/2006